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SHORT COMMUNICATION

# Seroprevalence of Rubella and Cytomegalia in Young Women from Biała Podlaska District

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Abstract

The aim of this study was to analyze the seroprevalence of rubella and cytomegalia among young women. The study included 175 healthy women from the Biała Podlaska District, aged 16 to 35 years. Anti-rubella and anti-CMV IgG were determined by ELISA. 172 (98.3%) study subjects tested positive for rubella antibodies, 1 (0.6%) was seroindeterminate and 2 (1.1%) were seronegative. CMV antibodies were detected in 119 (68.0%) participants; the series included also 1 (0.6%) seroindeterminate and 55 (31.4%) seronegative women. The levels of rubella and CMV antibodies were not significantly affected by age, place of residence and educational level of the study subjects.

K e y w o r d s: cytomegalovirus, *Rubella virus*, seroprevalence in women

*Rubella virus*, a pathogen from the *Togaviridae* family, is found solely in humans and causes rubella, a typical childhood disease. The virus is spread *via* airborne droplets containing respiratory secretions from an infected person. Children with rubella present with maculopapular or macular rash and lymph node swelling. Infection in adults is usually more severe, and may be associated with bone and joint pain. The most severe form of infection is congenital rubella associated with primary maternal infection during pregnancy. Congenital rubella may contribute to vision defects, deafness, cardiac anomalies, microcephalia, developmental disorders, fetal death or infant mortality during the 1st year of life. Transfer of maternal antibodies produced in response to infection or immunization protects fetus against rubella (Lambert *et al.*, 2015; Murray *et al.*, 2011).

*Human herpesvirus 5* (HHV-5), referred to as human cytomegalovirus (CMV, HCMV), is a lymphotropic virus from the *Herpesviridae* family, replicating in human fibroblasts, epithelial cells and macrophages. CMV establishes a latent infection in T-lymphocytes and macrophages. CMV may be spread with saliva, urine, breast milk, vaginal and cervical secretions, semen and blood. CMV infection may occur in utero; furthermore, the virus may be transmitted *via* oral and sexual route, during transfusions and organ transplantations. In immunocompetent persons, the infection is typically asymptomatic or has the form of a mild mononucleosis-like syndrome. However, it may become more severe in immunocompromised subjects or in patients on immunosuppressive treatment (Ludwig and Hengel, 2009; Murray *et al.*, 2011). Congenital CMV infection is considered to be the most common congenital transmissible disease in Europe. Primary maternal infection during pregnancy poses the highest risk of CMV transmission to the fetus. In seronegative women, the risk of primary infection approximates 1–8%, and in 32% of the cases results in fetal transmission of CMV. Up to 10–18% of infected neonates develop congenital CMV infection which may manifest with impaired psychomotor development, vision disorders, hearing loss or complete deafness. Whereas most of the infected neonates are asymptomatic at birth, 10–15% of them may develop late complications, typically hearing loss. Fetuses of seropositive women are usually protected by maternal CMV antibodies. However, even in such cases there is a 1.4% risk of fetal infection due to reactivation of a latent maternal infection with CMV or superinfection with another viral strain, and up to 8% of

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children infected in utero may suffer from hearing loss (Hamilton *et al.*, 2014; Kadambari *et al.*, 2011; Ludwig and Hengel, 2009).

The aim of the study was to analyze the seroprevalence of *Rubella virus* and cytomegalovirus antibodies among young women. The study included 175 healthy women from the Biała Podlaska District (Lublin Province, Poland), aged between 16 and 35 years (mean age 22.7 years). Women living in towns and villages constituted 46% (n = 80) and 54% (n = 95) of the study group, respectively. Fifty six (32%) study subjects declared having higher education; 118 (67%) women had completed secondary and 1 (1%) primary education. Blood samples were collected in May 2015.

The presence of anti-*Rubella virus* IgG was detected by ELISA (Anti-*Rubella virus* ELISA (IgG), Euroimmun, Germany). Microtiter wells were coated with antigens of *Rubella virus*. The results above or equal 11 relative units/ml (RU/ml) were considered as positive, below 8 RU/ml as negative, whereas borderline results were ≥ 8 and < 11 RU/ml. The presence of anti-CMV IgG was detected by ELISA (Anti-CMV ELISA (IgG), Euroimmun, Germany). Microtiter wells were coated with antigens of CMV. The results above or equal 22 RU/ml were considered as positive, below 16 RU/ml as negative, whereas borderline results were ≥ 16 and < 22 RU/ml. The tests were carried out and the results were interpreted according to the manufacturer's instructions.

The results were subjected to statistical analysis with Statistica v. 10 package. Significant differences in values of quantitative variables were identified with non-parametric Mann-Whitney U-test, with statistical significance threshold set at $p = 0.05$. The study protocol was approved by the Local Bioethics Committee at the Medical University of Lublin (decision no. KE-0254/183/2014).

One hundred seventy two (98.3%) study subjects tested positive for rubella antibodies, 1 (0.6%) was seroindeterminate and 2 (1.1%) were seronegative. CMV antibodies were detected in 119 (68.0%) participants; the series included also 1 (0.6%) seroindeterminate subject and 55 (31.4%) seronegative women. Detailed information about the antibody levels is presented in Table I. The levels of rubella and CMV antibodies were not significantly affected by age, place of residence and educational level of the study subjects.

According to the ECDC report on epidemiology of mumps and rubella, a total of 1 708 rubella cases were recorded in Europe between July 2015 and June 2016, and the vast majority of them (n = 1 553, 91%) were diagnosed in Poland. However, as emphasized by the authors of the report, only a very small proportion of the diagnoses (1.1%) were confirmed in a laboratory setting (ECDC 2016). In 1989–2002, active immunization with a monovalent rubella vaccine was obligatory solely for Polish girls. However, beginning in 2003, all Polish children, both girls and boys, need to be immunized with two doses of MMR (measles, mumps, rubella) combined vaccine at 2 and 10 years of age (Zimmerman *et al.*, 2011). According to the report published by the National Institute of Hygiene, MMR vaccination coverage in Poland is high, exceeding 95% in 2015 (Czarkowski *et al.*, 2015). Smits *et al.* (2014) presented a 32-year Dutch experience with MMR vaccine; the product proved to be effective, as long-term persistence of antibodies induced by vaccination was demonstrated in up to 95% of subjects who had received two doses of MMR.

The study conducted in 2000–2002 by Wysokińska *et al.* (2004) in a group of 15- to 30-year-old women (n = 1 289) from various regions of Poland, documented the presence of anti-rubella IgG > 15 IU/ml in 89.5% of the subjects. Also 98.3% of women participating in our study had rubella antibody levels ≥ 11 RU/ml. Currently, ≥ 10 IU/ml is considered a protective level of rubella antibodies (Lambert *et al.*, 2015). In view of the abovementioned findings, a considerable proportion of Polish children diagnosed with rubella solely on the basis of clinical presentation, may in fact suffer from other viral diseases that manifest with maculopapular rash, *e.g.* parvovirus B19 infection.

Table I
Titers of anti-*Rubella virus* and anti-CMV IgG depending on age

| Age | Number of persons (N) | Titers of anti-*Rubella virus* (RU/ml) | | | | Titers of anti-CMV (RU/ml) | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | $\bar{x}$ | SD | MIN | MAX | $\bar{x}$ | SD | MIN | MAX |
| ≤ 19 | 17 | 55.78 | 24.42 | 10.40 | 97.09 | 59.53 | 60.89 | < 2.00 | 167.78 |
| 20–21 | 73 | 82.48 | 53.21 | 6.96 | > 200.00 | 77.02 | 62.92 | < 2.00 | > 200.00 |
| 22–23 | 40 | 76.34 | 48.18 | 5.09 | > 200.00 | 77.58 | 64.63 | < 2.00 | > 200.00 |
| 24–25 | 14 | 117.14 | 63.63 | 29.00 | > 200.00 | 85.94 | 69.81 | < 2.00 | > 200.00 |
| 26–27 | 10 | 87.18 | 53.04 | 20.93 | 191.93 | 63.89 | 71.81 | < 2.00 | 199.14 |
| ≥ 28 | 21 | 98.02 | 60.46 | 11.21 | > 200.00 | 104.13 | 75.23 | < 2.00 | > 200.00 |
| Total | 175 | 83.39 | 53.10 | 5.09 | > 200.00 | 78.67 | 65.79 | < 2.00 | > 200.00 |

The seroprevalence of CMV antibodies among women of childbearing age ranges between 45% and 100%. The highest seroprevalence is reported in Africa, Asia and South America, and the lowest in Western Europe and United States. The seroprevalence increases with age; furthermore, it was shown to be higher in individuals with poor socioeconomic status and in non-white women (Cannon *et al.*, 2010). The seroprevalence of CMV antibodies in European women of childbearing age varies between 30% and 96%. The lowest seroprevalence rates were documented in Ireland (in native Irish women), Netherlands and Germany, and the highest in Turkey, United Kingdom in Asian women and Ireland in non-Irish immigrants (Ludwig and Hengel, 2009).

Gaj *et al.* (2012) analyzed the seroprevalence of CMV antibodies in pregnant women who have been hospitalized in two clinics in Łódź in 1999–2009. Anti-CMV IgG and IgM were detected in 76.7% and 13% of the study subjects, respectively. The seroprevalence of CMV antibodies was not influenced by age, parity and place of residence; however, anti-CMV IgG were detected less often in women examined in 2005–2009 than in those tested during the earlier period. In another study, conducted in 2010–2011, also among pregnant women from two hospitals in Łódź, Wujcicka *et al.* (2014) documented a 62.4% seroprevalence of anti-CMV IgG. The CMV antibodies were significantly more often found in women aged 36 years and older, with primary or vocational education, and in those having children. Siennicka *et al.* (2016) analyzed sera from 712 women aged between 15 and 49 years, and showed that the seroprevalence of CMV antibodies increased with age, from 74.3% in subjects younger than 30 years, to 94.3% in those older than 45 years. The seroprevalence was not affected by the place of residence of the study subjects. In our present study, the seroprevalence of anti-CMV IgG amounted to 68.0%. We did not observe statistically significant age-related differences in the antibody levels, probably due the fact that all the study subjects were younger than 36 years and most of them (92%) had no children. Nevertheless, these findings imply that Poland is a country with a moderate seroprevalence of CMV antibodies.

In conclusion, this study documented the high, up to 98.3% seroprevalence of rubella antibodies, which seems to confirm the effectiveness of the vaccination program that is currently used in Poland. 68.0% of the study subjects tested positively for anti-CMV IgG, which implies that Poland is a country with a moderate seroprevalence of cytomegalovirus antibodies.

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